

**Double Patenting Rejection**

As discussed in the response filed April 27, 2010, the rejection of claim 13 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent 7,485,654, has been rendered moot in view of the claim amendments, which are now entered as a result of the RCE. Withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. § 103, based on Hellberg in view of Lehmann**

As discussed in the response filed April 27, 2010, the rejection under 35 U.S.C. § 103, based on Hellberg in view of Lehmann, has been rendered moot in view of the claim amendments, which are now entered as a result of the RCE. Withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. § 103, based on Hellberg in view of Hara**

Claims 13 and 17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hellberg et al. (WO 03/020281) in view of Hara et al. (Protein kinase inhibition by fasudil hydrochloride promotes neurological recovery after spinal cord injury in rats).

This rejection is respectfully traversed.

Initially, Applicants respectfully request that the Examiner consider the remarks set forth on pages 5-7 of the response filed April 27, 2010. Further, Applicants provide the following additional comments for the Examiner's consideration.

Hellberg describes a method comprising administering neurotrophic factor stimulators, which increase the production or activity of neurotrophic factors (NGF, BDNF, NT-3, bFGF etc.), to a human patient, to promote neuron regeneration or neurite outgrowth, where the method is useful for the treatment of dry eye and corneal nerve damage. Accordingly, Hellberg indicates that the treatment is influenced by "neurotrophs". However, Hellberg fails to teach or suggest that treatment of dry eye and corneal nerve damage is related to the inhibition of ROCK. This is acknowledged by the Examiner, who admits that Hellberg fails to teach the use of Rho kinase inhibitors.

Hara teaches that fasudil hydrochloride shows neurological recovery after spinal cord injury (SCI). The Examiner holds that neurotrophic factors such as bFGF and NGF are

functionally equivalent neuro-promoters. However, Hara fails to mention the trigeminal nerve (corneal nerve).

The Journal of Comparative Neurology (P. Ozdinler et al., Vol. 438, pages 377-387, 2001, submitted with Applicants' IDS of January 13, 2006) describes that, in a rat cultured trigeminal tract, Rho activator (LPA) blocked NGF-induced axon outgrowth (Fig. 5E), and dominant negative Rho (RhoDN) increased in the mean axon number (Fig. 6C). However, the reference also describes that, in the absence of neurotrophic factors, activation or inactivation of one particular Rho GTPase may not be sufficient to change axonal outgrowth properties. (Please see page 385, left column, lines 2-5.)

As discussed in the fifth paragraph on page 2 of the response filed April 27, 2010, the presence of ROCK I and ROCK II in the trigeminal nerve (corneal nerve) cell was **not known before the filing date of the present application**. Thus, assuming, *arguendo*, that the combination of references suggests that neurotrophic factors can promote the neurite outgrowth of the trigeminal nerve, it would not have been obvious that ROCK inhibitor (which is **not** a neurotrophic factor) can promote neuritogenesis of the trigeminal nerve.

Accordingly, in view of the comments provided in the response filed April 27, 2010, as well as the additional comments set forth above, it is respectfully asserted that the present claims are patentable over the cited combination of references. Withdrawal of this rejection is respectfully requested.

**Conclusion**

Therefore, in view of the foregoing remarks, as well as the amendments and remarks submitted April 27, 2010, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Response, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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/Amy E. Schmid/

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